Chapter 15

Discussion and recommendations

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Introduction

15.1 More can and must be done to improve the quality of the debate about research involving animals. Some of those who oppose such research accuse those in favour of acting without any legitimate ethical motives, and vice versa. We hope that the discussion in Chapter 14 has helped to show that such generalisations are mistaken, and that a highly complex picture emerges when the various positions are taken seriously.

15.2 We observed that the positions are not categorically distinct, but should rather be viewed as positions on a spectrum. Within this spectrum there is a significant area of common ground, shared by all members of the Working Party, despite their differences with regard to other issues. We describe this area of agreement below in the form of a *consensus statement*. Several practical implications that follow are explained in more detail in the conclusions and recommendations which are based on the recognition that all animal research needs to be justified. We address:

- ways of improving the quality of debate about research involving animals in society (paragraphs 15.22–15.52);
- the role of legislation and regulation (paragraphs 15.53–15.56);
- the development and implementation of the Three Rs (paragraphs 15.57–15.62); and
- a range of more specific issues, which include:
  - ways of motivating and monitoring approaches to reduction of the use of animals in research (paragraphs 15.64–15.67),
  - issues raised by the possibility that research is duplicated (paragraphs 15.65–15.70),
  - the use of GM animals (paragraphs 15.71–15.75),
  - the scientific validity of animal experimentation (paragraphs 15.76–15.80),
  - toxicity testing (paragraphs 15.81–15.83),
  - problems in harmonising international test guidelines (paragraphs 15.84–15.87), and
  - UK researchers commissioning or undertaking research abroad (paragraphs 15.88-15.91).

Consensus statement by all members of the Working Party

Research involving animals and other uses of animals

15.3 It is important to consider the ethical issues raised by animal experimentation in the wider context of the other uses of animals in society, and to take into account:

- the impact on the lives and welfare of animals that different uses have;
- the broader consequences if there were a ban on using animals in specific circumstances;
- a comparison of the benefits arising from the different uses of animals; and
- the numbers of animals involved.

15.4 The involvement of animals in research cannot be justified simply by the fact that animals are used or abused in other ways. Each use requires special consideration. Members of the Working Party noted during their own discussions, and in considering responses to the Consultation, that views on animal research were not always consistent with views on the

other uses of animals. Awareness that contradictory views are often held simultaneously is an important first step in considering the ethical issues raised by research involving animals.

The benefits of research involving animals

15.5 Historically, animals have been used in a wide range of scientific research activities that have provided many benefits to society, particularly in relation to the advancement of scientific knowledge, human and veterinary medicine and the safety of chemical products.

15.6 Some of these advances might have been achieved by other means, although we cannot know this. Neither can we know what a world would look like in which animal research had never been undertaken. Hypothetically, there may have been other options that could have produced acceptable levels of knowledge and healthcare. These levels might have been lower than our current standards, but perhaps if society had deemed the use of animals for research as unacceptable there would have been acceptance of greater limitations on scientific and medical progress. Alternatively, it is conceivable that equally good or better progress might have been achieved with other methods. The Working Party agreed that speculation about whether or not acceptable standards in basic and applied research could have been achieved in the past by means other than the use of animals is less important than the question of assessing the consequences of continuing or abandoning animal experimentation now.

15.7 It is sometimes assumed that to end animal research would be to end scientific and medical progress, but such generalisation is unhelpful. The UK Government has responded to changes in the moral climate by introducing policies that have ended some types of animal research and testing in the UK. For example the use of animals for the testing of cosmetic products and their ingredients, alcohol and tobacco has ceased. Similar policies are in place regarding the use of the great apes. Independent of the moral acceptability of research, the scientific costs and benefits of abandoning specific types of animal research need to be assessed on a case by case basis. On the one hand, the possibility of the emergence of new diseases may require a reassessment of whether the abandonment of specific types of research is still justified. On the other, scientific advances that could replace the use of animals in some areas may enjoin us to assess whether further policies should be introduced to terminate these uses of animals accordingly.

15.8 The validity, usefulness and relevance of specific types of animal research, for example in relation to the use of animals for the study of human diseases, needs to be ascertained in each individual case.

Desirability of a world without animal research

15.9 All research licensed in the UK under the A(SP)A has the potential to cause pain, suffering, distress or lasting harm to the animals used. Most animals are killed at the end of experiments. A world in which the important benefits of such research could be achieved without causing pain, suffering, distress, lasting harm or death to animals involved in research must be the ultimate goal.

15.10 We have considered the different arguments advanced in favour of and against continuing specific types of animal research in Chapters 3 and 14. Some believe the imperative to protect animal welfare should be overriding, whereas others believe that the moral arguments favour the continuation of research on animals. All members of the Working Party acknowledged that these viewpoints arise from moral convictions that should be given serious consideration. This approach requires open-mindedness in trying to understand the reasons and arguments of others. Genuine willingness is also required to test and, where necessary, revise one's own moral framework.

15.11 While we trust that more progress in the moral debate can be made, we are aware that, for the near future, further moral argument alone cannot provide a universal answer as to whether or not research on animals is justified. But practical advances in scientific methods can reduce areas of conflict. For this reason, the importance of the Three Rs, and especially of the need to find Replacements, cannot be overstated.

The ethical importance of the Three Rs

15.12 The Working Party therefore concludes that it is crucial that the Three Rs are, and continue to be, enshrined in UK regulation on research involving animals. The principle that animals may only be used for research if there is no other way of obtaining the results anticipated from an experiment is also fundamental.[1] Furthermore, we observe that for moral justification of animal research it is insufficient to consider only those alternatives that are practicably available at the time of assessing a licence application. The question of why alternatives are not available, and what is required to make them available, must also be asked. The potential of the Three Rs is far from being exhausted. The Working Party therefore agrees that there is a moral imperative to develop as a priority scientifically rigorous and validated alternative methods for those areas in which Replacements do not currently exist. It is equally important to devise mechanisms that help in the practical implementation of available validated methods.

15.13 In applying the Three Rs it is crucial to consider not only the context of the experiments but also the many other factors that can affect animal welfare, including breeding, transportation, feeding, housing, and handling. The quality of these factors, and the ability of animals to satisfy their species-specific needs, can usually be improved.

Regulation

15.14 We acknowledge that the UK has the most detailed legislative framework regarding animal research in the world. But proper attention to the welfare of animals involved in research and the accountability of scientists who conduct animal research cannot be achieved merely by having detailed regulations. Regulation can act as an emotional screen between the researcher and an animal, possibly encouraging researchers to believe that simply to conform to regulations is to act in a moral way. It is therefore crucial to promote best practice more actively and to improve the culture of care in establishments licensed to conduct experiments on animals.

15.15 When considering the replacement of specific types of research by alternative methods, it is important to take account of the international context in which research involving animals takes place. Many chemical and pharmaceutical compounds that have been developed are being marketed in countries or regions that have different regulatory frameworks for animal research and testing. Alternatives have been internationally accepted for safety testing. Nonetheless, many Replacements are not universally accepted, and the process of validation is lengthy. These processes need to be optimised and initiatives aimed at abandoning and replacing specific types of animal testing at national levels complemented by initiatives at the international level. This is not to say that initiatives in the UK can only be taken once there is consensus at an international level. In the past, the UK has been a leader in working towards change in international policies related to research involving animals. This leadership should be encouraged.

1 A(SP)A, Section 5 (a).

Duplication of experiments on animals

15.16 Scientific experiments involving animals are sometimes repeated by the same or other research groups. In considering whether the repetition of experiments should take place, it is important to distinguish between *duplication* and *replication* of experiments:[2]

- Duplication of harmful animal experiments is in principle unacceptable. We use the term to describe cases where there is insufficient scientific justification for the repetition. It occurs primarily when the scientist either does not know that another has carried out the experiment or test in question, or when he does know but is unable to attain reasonable access to the information.
- Replication refers to repetition of experiments or tests when this is necessary for sound progress in scientific enquiries. The scientific method demands that research findings need to be corroborated by the same and other research groups in order to establish the validity of the results.

15.17 The Working Party acknowledges that academic competitiveness and commercial confidentiality can sometimes complicate the sharing of information. But at its best, science is an open process, and mechanisms that prevent the sharing of information need to be reviewed carefully in terms of their justification and implications for the use of animals in research.

The context of the debate

15.18 The majority of researchers who use animals consider that, despite progress in the implementation of the Three Rs, animal research will remain an essential part of their work. Furthermore, the current regulatory frameworks for approval of chemical products and medicines require tests involving animals. We conclude that it is unrealistic to assume that all experiments on animals will end in the short term. It is crucial, therefore, to create a climate in which the necessity and justification for using animals is assessed and discussed fairly, and with due respect for all views.

15.19 Constructive debate would be facilitated by the provision of clear information about the full implications of research involving animals in terms of the numbers and species of animals used, as well as the pain, suffering and distress to which they are subjected. It is also important that society should be informed about the scientific, medical and other benefits of animal research. Information about selected aspects of research without provision of any further context can be misleading.

15.20 All members of the Working Party agreed that the use of violence and intimidation against members of the research community, research institutions, their business partners, family and neighbours, or against organisations and individuals representing animal welfare groups, is morally wrong and politically insidious. The freedom to promote or oppose research involving animals peacefully and democratically, however, must be maintained.

Conclusions and recommendations

15.21 Before we present the conclusions and recommendations, we must clarify two important points:

- Members of the Working Party who believe that research using animals is, on balance, justified, as well as those members who take the view that it poses a moral dilemma,

2 Animals are sometimes used in repeated experiments for the purpose of education or training. We have not addressed the issues raised by this particular use, see paragraph 1.18.

find most research which is currently undertaken to be acceptable. They are cautious of any proposals that might undermine progress in basic and applied sciences which, they believe, in specific areas crucially depends on research involving animals. Other members who, within the spectrum of possible views, are closer to the abolitionist view, are implacably opposed to the use of sentient animals for any scientific or medical purposes, and assert that other methods must be used to ensure progress. They are equally cautious of any proposals that prolong or legitimise the infliction of pain and suffering on sentient animals. We emphasise that the recommendations that follow below, several of which aim to improve the conditions in which animals are used, should not be taken to imply the acquiescence of the latter group to animal experimentation. These members acknowledge that animals are currently subjected to experiments and believe that they need protection. While they continue to advocate that the recommendations should go further in specific areas, they accept them as steps in the right direction, without endorsing research involving animals in principle.

- Because of the diversity of views and beliefs within the Working Party, it has not been possible to achieve complete agreement on all of the recommendations by all members of the group. In our discussions, however, and in discussion with the Council, it became clear that in the context of a highly polarised debate it is crucial to make unambiguous recommendations in specific areas. While it is therefore not possible to attribute to all members of the group the conclusions and recommendations presented on any one issue, all members do accept the recommendations as valid contributions to the debate, clarifying further important implications of the more abstract thoughts presented in the consensus statement above. Nonetheless, on a few occasions it did not prove possible to identify positions that were acceptable to all members. In such instances we have tried to explain the reasons why some members could not agree with particular conclusions or recommendations. We hope that the descriptions of disagreement help to clarify the nature of the underlying dispute in a constructive way.

The context of the debate

General observations

15.22 Members of the research community who use animals in their work frequently refer to evidence from opinion polls to support their claim that most people support research on animals because of the benefits to humans. They take the view that more information on the benefits of research involving animals would help engender further support from the public. Those who are fundamentally opposed to research involving animals, and those who are primarily concerned about the pain and suffering it may cause, also use evidence from opinion polls to support their views. They often claim that most people would share their views if only they knew more about the welfare implications of research. While evidence from opinion polls should be treated with some caution (paragraph 1.16), many people would like more information on research involving animals, some asserting that it takes place in secret (see paragraph 2.19).

15.23 One response to this situation would be to improve transparency and openness, which should serve the interests of all the various parties concerned with issues raised by animal research. Freedom of information is crucial to informed debate in democratic pluralistic societies (paragraph 14.63). Increased openness and transparency should therefore be encouraged, subject to safeguards for confidentiality of proprietary information and assurances that the safety and security of those involved in animal experimentation will not be compromised. Such an approach would also be consistent with the requirements of the FoI Act (Box 13.4).

15.24 We therefore consider first how provision of information by the Home Office can be improved, especially in relation to the presentation of the *Statistics*, details about granted licences for research and the way the cost-benefit assessment is carried out. We then explore ways in which discussion between those involved in research and interested stakeholders can be improved; consider issues raised by the conduct of public debates on animal experimentation; and review the role of scientists, campaigning organisations and teachers in education and higher education. We also comment on the practice of using violence and intimidation as means of protest against animal research.

Provision of information by the Home Office

Statistical information about the number of animals used and the suffering involved

15.25 The *Annual Statistics of Scientific Procedures on Animals,* published by the Home Office, have an important role in providing information about animal experimentation. At the same time, there is wide agreement that the data are presented in ways that are not readily accessible to lay people, and that the presentation could be improved. In particular, the *Statistics* have been criticised for not providing clear answers to the following questions: (i) what is the nature, level and duration of pain, suffering and distress actually experienced by animals used in the different kinds of procedures? and (ii) how many animals are used in procedures and related activities?

15.26 It is not possible to answer the first question, because information about welfare implications is only provided prospectively, in the process of the licence application (see paragraph 13.14). By definition, it is not possible to know in advance how animals will be affected in practice, and data from separate interim or retrospective analyses are not reported publicly.

15.27 Information about the degree of pain and suffering can, in some sense, be inferred from the *Statistics* about the severity bands assigned to granted project licences. These are classified in one of three bands: *mild, moderate* or *substantial* (see Box 13.3). But over the five-year period of a project licence, a range of different protocols, themselves assigned different severity limits, may be carried out. It is questionable how meaningful it is to average out the different limits under one band, in order to provide the public with accurate information. For example, it may be the case that a project that contains ten mild protocols, each involving 10,000 animals, and one protocol with a substantial severity limit involving 50 animals, would still be classified as mild.[3] Furthermore, it has also been suggested that the category of moderate protocols 'appears to be something of a catchall, covering a wide range of the more invasive procedures'.[4] We make the following observations.

15.28 Information about the suffering that animals involved in procedures experience in practice is unsatisfactory. **We recommend that the Home Office should make retrospective information about the level of suffering involved during procedures publicly available. In gathering this information the Home Office should also obtain and make available, retrospectively, information about the extent to which the scientific objectives set out in applications have been achieved.**

3 Animals Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p44, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

4 Animals Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p44, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

15.29 The terminology used to describe the severity of projects and individual protocols and procedures is not straightforward and therefore difficult for members of the public to understand. **We recommend that the annual *Statistics* should provide case studies of projects and procedures that were categorised as *unclassified, mild, moderate* or *substantial*. Case studies should also include examples of animals used over extended periods of time and should describe not only their immediate involvement in research but also the range of factors that influenced their life experiences, such as the conditions of breeding, housing and handling** (see paragraph 4.31).

15.30 **The current system of severity banding for project licences and the severity limits for procedures should be reviewed, particularly the use of the *moderate* category which covers a wide range of different implications for animal welfare. For the general public, the category *unclassified*, which refers to protocols and procedures involving terminally anaesthetised animals, is too vague to be informative, and should be clarified.**[5]

15.31 The *Statistics* give details about the total number of *animals* used for the first time in a year, and the total number of *procedures* initiated in that year (paragraph 13.27). As we have said, the term *procedure* refers to a wide range of activities, with very different implications for animal welfare which may arise from breeding, the withdrawal of blood, or experiments where death can be the endpoint. It is not straightforward to infer from the number of procedures undertaken how many animals have experienced what kind of pain, suffering or distress.

15.32 The humane killing of animals by means set out in Schedule 1 of the A(SP)A, for whatever purpose, is not itself a licensed procedure. Animals killed in this way are therefore not recorded in the *Statistics*. Many would argue that possession of a life is a morally relevant feature, and that it is therefore important to provide information about the number of animals that are killed humanely (paragraphs 3.47, 13.26 and 14.5).

15.33 We realise that the system of collecting data about the numbers of animals used in research is very complex and that care needs to be taken to avoid making existing administrative processes more onerous. **Nevertheless, we think it highly desirable to present clearer information about how many animals of a particular species experience pain, suffering and distress, to what degree, and for how long. We therefore recommend that the *Statistics* be revised to provide this information, including details about the number of animals killed under A(SP)A Schedule 1.**

15.34 Further thought is required to identify how changes could be made to improve information about the suffering and numbers of animals involved in research. We are aware that the APC,[6] LASA and the RSPCA together with the Boyd Group[7] are considering these issues at the time of writing. We hope that the Home Office will find our general observations useful in considering the reports from these groups.

Information about licensed research projects

15.35 There has been some discussion about whether or not, and if so to what degree, information about research projects that have been approved by the Home Office should

5 We note that some explanation can be found in the *Guidance notes* on the A(SP)A (p32). However, it is unlikely that members of the public will consult this document, and it is therefore important to clarify the terminology in appropriate places, for example in the *Statistics*.

6 The APC's Report will be available in 2005 at: http://www.apc.gov.uk/reference/reports.htm. See Animal Procedures Committee (2004) *Work Programme*, available at: http://www.apc.gov.uk/aboutapc/workprog2004.htm. Accessed on: 21 April 2005.

7 See http://www.boyd-group.demon.co.uk, see also: The Boyd Group (2004) *Categorising the severity of scientific procedures on animals - Summary and reports from three round-table discussions on the use of severity limits and bands in the UK*, available at: http://www.boyd-group.demon.co.uk/severity_report.pdf. Accessed on: 21 April 2005.

be made available to the public. We note that, following an announcement by the Government in 2004,[8] the Home Office has made available the first anonymised information in the form of *Abstracts of Project Licences*[9] in January 2005. **We welcome the principle of publishing more information, and the decision to make it available in a searchable and publicly accessible database in due course.** We also note that the information provided in the first *Abstracts* varies in content, level of detail and style of presentation. We therefore **recommend that the current form of presentation be reconsidered, to ensure that, as far as possible, meaningful information about the following categories is provided:**

- **the goals and predicted benefits of research;**
- **the probability of achieving these goals;**
- **the numbers and species of animals to be used, and an explanation of why they are needed at this stage in the project;**
- **what is likely to happen to the animals during the course of the project, including adverse effects from husbandry, supply, transport and procedures;**
- **what consideration has been given to the Three Rs to achieve all or part of the research objective(s), and how they have been applied;**
- **on what grounds possible alternatives have been rejected;**
- **source(s) of funding (i.e. public, private or both).**

15.36 Members of the Working Party were unable to agree in which form this information should be provided. While there was a range of views, those at the two ends of the spectrum were as follows:

- Some members, concurring with the views of several animal protection groups, argue that full project licences should be made available, in which only the names of researchers, research facilities and commercially sensitive information have been removed. They believe that this step would be a correct interpretation of the FoI Act (see Box 13.4), and that any further editing of licences would reduce trust in the Home Office, which might otherwise be suspected of operating in non-transparent ways. They assert that access to full, anonymised licences is necessary to allow the public to gauge the extent of costs to animals, to allow review and challenge of the information and to comment on the way in which the cost-benefit assessment has been made.[10]
- Other members, noting that their view would be shared by most researchers using animals, consider that the current format is, in principle, suitable, although they would like to see less rather than more information made public. Hence, they wish to keep the new practice under close review. They argue that the legislative framework already requires assessment of the acceptability of research by the ERP and the Home Office, and that participation by the public in the regulatory system is not permitted. This

8 Home Office (2004) *Ministerial statement announcing the outcome of the review of section 24 of the Animals (Scientific Procedures) Act 1986*, 1 July 2004, available at: http://www.homeoffice.gov.uk/docs3/animalproc_wms_section24_040701.pdf. Accessed on: 4 April 2005.

9 Home Office (2005) *Abstracts of project licences granted under the 1986 Act*, available at: http://www.homeoffice.gov.uk/docs4/abs_projectlicences0.pdf. Accessed on: 21 April 2005. The Home Office has previously released details of ten project licences under a Code of Practice which preceded the FoI, see Box 13.4.

10 See, for example, BUAV (2005) *Government in ruse to thwart Freedom of Information Act*, available at: http://www.buav.org/press/2005/01-01.htm. Accessed on: 21 April 2005; NAVS (2003) Freedom of information & animal experiments, available at: http://www.navs.org.uk/news/politics/foi.htm. Accessed on 21 April 2005.

system of assessment, together with the assessments made by the researchers themselves, and the funding bodies, is judged to be sufficient. The possibility of increased openness is viewed with scepticism because of fears about compromising accepted standards of confidentiality and commercial and academic competitiveness. Researchers using animals are also concerned that more detailed information about specific research projects could be used by militant activists to identify individuals and research facilities as potential targets.[11] They also argue that the provision of information contained in full, anonymised project licences would not be intelligible and informative to the public, and that shorter summaries would therefore be more effective in providing the public with information.

Information about the cost-benefit assessment

15.37 The common emphasis on the cost-benefit assessment in combination with the system of classification of severity bands sometimes evokes the impression that the Home Office assesses the costs and benefits of each individual experiment or procedure. As we have explained, this is not the case, since assessments take place at the much higher level of protocols and project licences (Box 13.3).[12]

15.38 The APC's 2003 Report, *Review of cost-benefit assessment in the use of animals in research*, provides very useful information about the application of the cost-benefit assessment in practice.[13] The Report also observes that relevant information is spread across several different documents, and recommends that **'there is a need for an easy-to-use, comprehensive list of factors to be taken into account in assessing costs, benefits and scientific validity, that could guide researchers and others engaged in ethical review under the act, such as members of ERPs.'**[14] **We endorse this recommendation.** Since ERPs should, ideally, also include lay people, it is important that this information is provided in a way that is accessible to non-experts. **Such a document would also be of use to the general public and the same information therefore should be provided in an accessible manner on the websites of the Home Office for the general public.** These materials should include specific case studies and also a summary of the *process* of how decisions are made in practice (see paragraph13.16 and Figure 13.1). We address further practical issues concerning the operation of the cost-benefit assessment below (paragraphs 15.54 and 15.56).

Provision of information by campaigning organisations and researchers, and ways of improving the broader context of public debate

Balanced information about animal research

15.39 Responses to our Consultation, and information in the press, indicate that there is still much confusion about the use of animals in research. Information which is publicly available can be unbalanced and biased. Although there are many excellent examples of responsible accounts of research involving animals, some animal protection groups sometimes use disturbing pictures that are not representative of the range of research that is permitted under current

11 News (2004) Science fears attacks will rise with Act *THES* 1657 10 September, p1.

12 See also *Guidance on the Operation of the A(SP)A 1986*, Appendix I, available at: http://www.archive.official-documents.co.uk/document/hoc/321/321-xi.htm. Accessed on: 6 May 2005.

13 The criteria for making cost-benefit assessments are discussed in Chapters 3 and 4 of the APC's report (see especially Chapter 4, Boxes 4.4, 4.5 and 4.6); A description of those involved at particular stages of processing a licence application is provided in Chapter 5. Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

14 Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p73, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

regulations.[15] Equally, some of the information that is produced by organisations representing those whose work involves animals focuses disproportionately on the medical benefits of animal research, paying less attention to areas such as basic research or product testing, and the pain and suffering experienced by animals involved in such uses.[16]

15.40 We encourage animal protection groups and organisations representing those involved in research using animals to produce fair and balanced literature on this subject. This should include, among other things, detailed information about both the scientific benefits and the costs in terms of the implications for animal welfare. Similarly, the advantages and limitations of using alternative methods for research need to be discussed in a realistic manner.

15.41 Public debates about research on animals would also be enhanced by educating young people about issues raised by animal experimentation through presenting all sides of the argument. More balanced materials could make an important contribution to an improved understanding of the costs and benefits, to both humans and animals, of research involving animals, particularly for use in schools. **We therefore recommend that the UK Department for Education and Skills should commission an academic department of education that does not have close links to pressure groups or to those involved in animal research, to produce suitable materials for use across the curriculum as appropriate, especially at Key Stages 2 and 3.**

Public debates and discussions in stakeholder fora

15.42 Much can be learned from meetings which provide a forum for dialogue and allow members of the public to discuss their views with relevant experts. **We welcome provision in the Government's Science & Innovation Investment Framework 2004–2014 for a new grants scheme 'to build the capacity of citizens, the science community and policy makers to engage in the dialogue necessary to establish and maintain public confidence in making better choices about critical new areas in science and technology.'**[17] We are aware that the way the grants scheme is operated is currently being reviewed, and that Ministers may decide to allocate funding for prioritised areas. **In view of our observation about the need to improve the quality of the debate, and also the Governments discussion about animal research in the Science & Innovation Investment Framework programme,**[18] **we recommend that funding should be provided by the Government to identify and carry out novel ways of achieving stakeholder engagement and public debate on issues raised by research involving animals. The Office of Science and Technology (OST) should liaise with the APC and the NC3Rs to advise Ministers on areas of particular concern.**

15.43 However, arranging dialogue, including public debates, on controversial matters is not straightforward. For example, there was some criticism of the Government's *GM Nation?*

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15 The Advertising Standards Agency has upheld several complaints made by the RDS about the use of unrepresentative pictures in campaigns. These include rulings against Naturewatch (October 1996), Uncaged campaigns (March 1998), Save the Hillgrove Cats (August 1999), FAUNA (September 1999) and Save the Newchurch Guinea Pigs (March 2000).

16 For example, some members of the Working Party consider that information brochures such as *Medical Advances from Research using Animals* (CMP 2003/4), *Animal Research and Human Medicine* (ABPI 2004) or *The Use of Non-human Animals in Research: A guide for scientists* (Royal Society, 2003), available at: http://www.royalsoc.ac.uk/policy/AnimalsResearch.htm Accessed on: 21 April 2005, which are intended to provide neutral information about animal research, are insufficiently balanced. See also Russell WMS (2004) The use of non-human animals in research: a guide for scientists *ATLA* **32**: 119–20.

17 See HM Treasury/DTI/Department for education and skills (2004) *Science & Innovation Investment Framework 2004-2014*, paragraph 21, available at: http://www.hm-treasury.gov.uk/media/33A/AB/spend04_sciencedoc_1_090704.pdf. Accessed on: 21 April 2005.

18 See HM Treasury/DTI/Department for education and skills (2004) *Science & Innovation Investment Framework 2004-2014*, paragraph 6.16-7.20, available at: http://www.hm-treasury.gov.uk/media/33A/AB/spend04_sciencedoc_1_090704.pdf. Accessed on: 21 April 2005.

debate which was organised in 2003.[19] There are a number of different approaches to be considered, from large public meetings to consensus conferences and citizens' juries. While we do not give detailed attention as to which approach might be best suited to discussion of issues raised by animal research we make some general observations.

15.44 First, it is important to create an environment for debate in which all views are heard and all participants are treated with the same respect. Secondly, the purpose and outcome of any public meeting or debate needs to be clear from the outset. For example, it might need to be stated whether the purpose is restricted to stimulating exchange of views, or whether it is being undertaken in the context of informing decision-making processes. Failure to consider the appropriate approach and outcome of any such exercise can possibly lead to more, rather than less, polarisation as well as to increasing scepticism about public-engagement exercises and trust in democratic processes.

15.45 In addition to public events, there are a number of *ad hoc* and permanent stakeholder groups that enable discussion among stakeholders. In our own debates, we realised the importance of having members who between them represent a broad spectrum of views on research involving animals. This approach allowed for comprehensive consideration of relevant arguments about specific areas of research. We encourage all parties to continue to take part in such fora.

Research on views of the public

15.46 We have already commented on the limitations of opinion polls, and the scarcity of peer-reviewed academic research, which could help provide reliable assessments to be made about the views of members of the public about research involving animals (paragraphs 1.14–1.16). Such information can be important in considering whether or not policies are likely to be supported by the majority of the population. **We therefore recommend that the Economic and Social Research Council (ESRC) and other relevant funding bodies provide funding for research to be undertaken on the knowledge, opinions and views of members of the public on animal research, and their underlying ways of reasoning.** Particular attention should be paid to the level and quality of information that participants have prior to, and while taking part in, the research, and to the ways in which provision of information affects individual responses.

Violence and intimidation

15.47 The current climate in which animal research takes place has been influenced by several factors, including protests that often entail threats, harassment and violence (paragraphs 2.22–2.24). The effects of these actions have been highly disproportionate to the very small number of activists involved.[20]

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19 Environment, Food and Rural Affairs Committee (2003) *Eighteenth Report*, available at: http://www.publications.parliament.uk/pa/cm200203/cmselect/cmenvfru/1220/122002.htm. Accessed on: 21 April 2005; Understanding Risk Team, University of East Anglia (2004) *A Deliberative Future? An Independent Evaluation of the GM Nation? Public Debate about the Possible Commercialisation of Transgenic Crops in Britain, 2003, Working Paper 04-02, University of East Anglia*, available at: http://www.uea.ac.uk/env/pur/latest_news.html. Accessed on: 21 April 2005.

20 Militant extremists have brought considerable fear to the lives of those whose work involves research on animals, and to their families. Many people who do not have direct association with animal laboratories but who work for institutions that provide services that facilitate animal experimentation have also been affected. Similarly, several charities which fund research involving animals have stated that they do not wish to engage in an open dialogue about the legitimacy of research on animals for fear of becoming a target for extremists. Animal rights extremists threaten not only scientists engaged directly in research, but also those working for legitimate animal welfare organizations such as the RSPCA and professional bodies such as the IAT and LASA. For example, for the past four years, the IAT has not been able to hold its annual conference in the UK because of threats from extremists. LASA has also had to hold all its meetings in undisclosed locations to minimise the attention of militant protestors. See also Home Office/DTI (2004) *Animal Welfare – Human Rights: protecting people from animal rights extremists*, available at: http://www.homeoffice.gov.uk/docs3/humanrights.pdf. Accessed on: 21 April 2005.

15.48 It is tempting to dismiss animal rights extremism as being wholly unwarranted. Yet those who resort to violence maintain they have the moral high ground. This can be frustrating to those who campaign within strictly constitutional limits, and who fear that violent and abusive actions damage their legitimate cause. Those who promote violence and intimidation to pursue their case against animal research often attempt to justify their actions on the basis that they are liberating animals in much the same way as the Allies liberated Europe from the Nazis. They believe the democratic process is too slow, and moreover that the voting system is invalid, in that animals are disenfranchised. In the wake of their activities are others who would not themselves use violence but who are prepared to threaten it, persuading themselves that bullying is acceptable because it is aimed at people who are bullying animals.

15.49 If some of those engaged in the animal rights movement were able to force research abroad or prevent multinational companies from opting to conduct work in the UK, by means of militant actions, they would claim such outcomes as a victory.[21] During our fact-finding meetings we heard different accounts of the effects of the actions of groups involved. Some of those working in the pharmaceutical industry and the contract research sector said that the presence of animal rights extremism was not a major factor in considering whether or not to opt for a different research location. But there have also been reports to the opposite effect, and attention has been drawn to possible economic and scientific setbacks for the UK, should protestors be able to continue their activities.[22] In 2004, multinational companies repeatedly urged the UK Government to amend the legal framework applicable to animal rights-related extremism, emphasising that the *status quo* was unacceptable and might influence decisions about investment. In 2005 the UK Government responded by making amendments to the Serious Organised Crime and Police Bill.[23]

15.50 **We conclude that all approaches based on violence and intimidation are morally wrong:** democracy is a precious achievement that allows conflict to be resolved without recourse to violence. It cannot permit exceptions where militant activities displace debate and consensus, otherwise anyone with any strongly held view would be able to prevail over the majority. The debate about animal experimentation must be conducted in a reasonable and civilised manner. Seeking to force research out of the country is not a solution to the complex issues it raises. We therefore fully concur on the issue of militant protest with one of the leading animal rights advocates, Professor Peter Singer:

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21 See, for example the Initiative *Gateway to Hell*, available at: http://www.gatewaytohell.net. Accessed on April 21 2005.

22 According to the ABPI, more than 65,000 people are directly employed by the pharmaceutical sector and a further 250,000 are dependent on it for their employment. In 2003, the industry contributed £2bn to the UK economy and generated exports of £7bn and a trade surplus of £2.3bn, the third highest after power generation and oil products. Members of the ABPI spend a combined £30–70 million a year on security, see Hennock M (2004) Pharma firms take on the extremists *BBC News online*, available at: http://news.bbc.co.uk/1/hi/business/3933939.stm. Accessed on 21 April 2005; Evans M (2004) Extremist animal rights activists pose main threat to economy *The Times online*, available at: http://www.timesonline.co.uk/article/0,,2-1396891,00.html. Accessed on 21 April 2005.

23 The Bill received Royal assent on 11 April 2005 and thus became the Serious Organised Crime and Police Act 2005, available at: http://www.uk-legislation.hmso.gov.uk/acts/acts2005/20050015.htm. Accessed on: 5 May. Sections 145–149 make it a criminal offence to cause 'economic damage' by means of organised campaigns of intimidation. They are intended to improve the enforcement of legal sanctions of attacks against businesses, company employees and their family members, charity shops and universities. In addition to other measures in the Act, new offences are introduced to respond to typical forms of protests. These include a new offence of protesting outside someone's home in such a way that causes harassment, alarm or distress to residents. There are additional powers for a constable to direct a protestor to leave the vicinity of a home and not return within such period as the constable may specify, up to three months. Individuals guilty of an offence under section 142 or 143 are liable, on summary conviction, to imprisonment for a term not exceeding 12 months or to a fine not exceeding the statutory maximum, or to both, on conviction on indictment, to imprisonment for a term not exceeding five years or to a fine, or to both. Since these provisions were agreed after the final meeting of the Working Party, we do not comment on the appropriateness of the Act, although in principle we welcome regulations seeking to prevent harassment and intimidation.

> 'I cannot support the use of violence in the cause of animal liberation. It sets a dangerous precedent – or, one might say, it follows dangerous precedents. In the United States, 'pro-life' extremists have fire-bombed abortion clinics and murdered doctors who terminate pregnancies. I consider these defenders of the sanctity of human life from conception to be misguided; but no doubt they are just as sincere in their convictions as defenders of animals. It is difficult to find democratic principles that would allow one group to use intimidation and violence, and deny the same methods to the other.'[24]

Open laboratories

15.51 In a highly polarised debate where many people hold strong views, the only option for making progress is for all concerned to engage in debate fairly and respectfully. Members of the public should have the opportunity to discuss animal experiments with researchers, and to visit laboratories to see the facilities and the animals that are being used. We realise that this suggestion raises a number of practical issues. It would be unacceptable if visitors to laboratory facilities abused the opportunity by protesting against research involving animals, using argumentative or unruly behaviour or by gathering intelligence so as to cause damage to property or harm to staff. Laboratories need to ensure that visitors have no such aims. Measures are also needed to prevent the exposure of visitors to allergens and to ensure that they do not disturb animals or spread infections.

15.52 Despite these possible problems, and the fears of members of the research community of being targeted by militant protestors, some academic and industrial scientists and scientific institutions involved in animal research are willing to engage with the public (see paragraph 2.30). Others are reluctant to do so. The Working Party experienced the fragile climate of trust at first hand, as it was not possible for all members who wished to attend fact-finding meetings at research facilities to do so (see Appendix 4). We take the view that in order to improve and sustain public trust, researchers at animal research facilities must find more ways to open themselves to dialogue. **We therefore recommend that those involved in animal experimentation should take a proactive stance with regard to explaining their research, the reasons for conducting it, the actual implications for the animals involved and the beneficial outcomes they intend for society.** These discussions should take the form of a two-way process, in which scientists not only inform the public about their research, but also listen to and understand concerns by members of the public.

The role of legislation and regulation

15.53 We learned from some of our discussions with representatives of patient groups that reference frequently is being made to the provisions of the A(SP)A, so as to allay concerns by members and non-members about animal research. Whether or not such referrals are suitable for the purpose depends not only on the formal provisions of the law, but also on its application in practice. Many animal protection organisations and respondents to the Consultation expressed concerns about the implementation of the provisions of the A(SP)A and quoted what they believed to be examples of ineffective regulation.[25] In contrast, many members of the research community who submitted comments were concerned about

24 Singer P (2004) Humans are sentient too *The Guardian* 30 July, p21.

25 Those critical of the implementation of the A(SP)A point to a number of reports which draw attention to claimed inadequacies in the implementation of the A(SP)A and they emphasise that the House of Lords Report concluded that the Home Office Inspectorate should be subject to periodic review, by a body other than the Inspectorate itself. See House of Lords Select Committee (2002) *Animals in Scientific Procedures* (Norwich: TSO), paragraph 5.13, Chapter 2, Box 2.9, and Lyons D (2004) *In a collapsed state – Imutran xenotransplantation research: a case study of Home Office enforcement of animal experimentation legislation, Uncaged campaigns*, available at: http://www.uncaged.co.uk/. Accessed on 21 April 2005.

what they perceived to be overly detailed and burdensome regulation.[26] A thorough review of regulation is beyond the scope of this Report and is being considered by other bodies.[27] Nonetheless, we offer some general observations below.[28]

Cost-benefit assessment and moral agency

15.54 The cost-benefit assessment is at the heart of the regulation of research on animals in the UK. There is sometimes the view that the assessment is only being carried out by the Home Office, which 'tells the researchers what to do' once it has decided on whether or not a licence application fulfils the criteria of the A(SP)A and is thus, from the regulator's point of view, acceptable. The APC's 2003 Report *Review of cost-benefit assessment in the use of animals in research* observed that this interpretation would be simplistic, since other individuals and committees are involved in assessing directly or indirectly the costs and benefits of a project (paragraph 13.16). The APC therefore emphasised that:

> 'project licence holders and others involved in study design and initiation bear responsibility for clearly setting out the costs and benefits of their research and carrying out cost-benefit assessments of their work, including critical evaluation of the need for animal studies at all. The roles of other bodies, such as the Home Office, ERP, and, where relevant, APC, are to evaluate, advise, and in some cases adjudicate the researchers' own cost-benefit assessments.'[29]

15.55 We welcome this clarification, which is compatible with our discussion about moral agency (paragraph 3.69). As we have said, it would be wrong to perceive acting morally simply as following rules. Instead, active and continued scrutiny of the costs and benefits is required from all those involved, before, during and after research. This responsibility cannot be devolved to regulators, and, as the APC has emphasised, the system is not intended to function in this way.

15.56 The APC's clarification underlines the importance of clear guidance on how to make cost-benefit assessments. Furthermore, it implies that both funding bodies and peer reviewers who may be involved in assessing licence applications have to take their responsibilities in the review process seriously. **We recommend that those involved in reviewing research proposals** (see Figure 13.1) **at every stage prior to submission to the Home Office consider not only the scientific aspects, but also animal welfare in appropriate detail**. Good science and good animal welfare are closely interrelated, and it would be wrong for the scientific review process to ignore animal welfare issues. We are aware that many funding bodies recognise this fact. In addition to assessments by internal review boards, some, such as the Wellcome Trust and the MRC routinely invite external reviewers to comment on welfare issues and the way the Three Rs are considered in research proposals involving the use of

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26 In support of claims that the implementation of the A(SP)A leads to excessive bureaucracy, researchers involved in animal experimentation have drawn attention to a number of recent reports including the House of Lords Select Committee Report, which concluded that 'The UK should strive not for the tightest regulation, but for the best regulation, properly enforced', They have also highlighted several recommendations made in this area by the Select Committee including the simplifying and shortening of project licences forms, and allowing the ERP to have the authority to approve routine or minor amendments. see House of Lords Select Committee (2002) *Animals in Scientific Procedures* (Norwich: TSO), paragraphs 5.33, 5.40, 6.11; Expert Group on Efficient Regulation (2001) *The Regulation of the Use of Animals in Scientific Procedures* (London).

27 See, for example, Reports by the APC (available at: http://www.apc.gov.uk), or the Boyd Group (available at: http://www.boyd-group.demon.co.uk).

28 Issues arising from different legislative and regulatory requirements in other countries, and problems in harmonising guidance internationally are discussed in paragraphs 15.84-15.91.

29 Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p77, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 Apr 2005.

animals. However, **there is anecdotal evidence that this practice is not universal, and we recommend that other funding bodies review their approach**.

Development and implementation of the Three Rs

15.57 We have observed that the Three Rs have a crucial role in the ethical justification of research. With regard to Replacements we concluded that it is necessary to ask the question of why Replacements in specific research areas are not available, and what is required to make them so (paragraph 3.63 and 11.19–11.30). A slightly different situation prevails with regard to Refinement and Reduction in that relevant information about these strategies exists in many areas, but their use and application is not sufficiently widespread. We referred to research showing that there is some variance in the application of Refinement,[30] and we also identified possible barriers, highlighting scientific, regulatory, organisational, and resource factors (paragraphs 12.23–12.28), all of which can have impact on the implementation of Refinement methods. Below we present our conclusions and recommendations with regard to improving the application of the Three Rs.

Publishing information about the Three Rs

15.58 Many members of the research community emphasise that, wherever possible, they implement the Three Rs, often exceeding regulatory requirements. In some cases, advances are made by individual researchers, but knowledge of improved practices tends to be limited to colleagues in the research establishment, and may not always be disseminated nationally or internationally in a systematic manner. In order to improve knowledge about and awareness of the Three Rs **we recommend that all journals publishing results of research involving animals consider the inclusion of a category on the Three Rs in the methodology section**.[31] Many journals now also provide supplementary information for articles on websites, and details about the implementation on Three Rs could be provided in this way.

Coordination of efforts between funding bodies and the NC3Rs

15.59 Medical research charities and research councils fund a large amount of animal research and should be encouraged to take more responsibility for the promotion and implementation of the Three Rs. Further to recommending that external reviewers comment on the way the Three Rs have been implemented in funding proposals (paragraph 15.56), we consider that those who fund research have two additional responsibilities. **First, in order to improve a systematic application of the Three Rs, funding bodies should request that for each project that receives funding, a short summary be submitted to the NC3Rs which describes the way in which the Three Rs were implemented in the project, which obstacles were encountered and how they might be overcome in the future.** This information would be useful to the NC3Rs in promoting exchange of experience and fostering best practice. **Secondly, based on this information, and in consultation with the NC3Rs, funding bodies should encourage funding applications for Three R-related research in areas that pose challenges.**

Enhancing the role of the Ethical Review Process (ERP)

30 See Richardson CA, Flecknell PA (2005) Anaesthesia and Post-operative Analgesia Following Experimental Surgery in Laboratory Rodents: Are we making Progress? *ATLA* **33**: 119–127; paragraph 12.26.

31 In a different context, one journal has recently reviewed its policy on the provision of information about statistical methodology in published articles. Research had revealed that this information was of varying quality, and the editors therefore decided to introduce a requirement for authors to submit specific information about statistical methods used in the methodology section of each article, see Editorial (2005) Statistically significant *Nat Med* **11**: 1-1.

15.60 The ERP has the potential to make a greater contribution to the identification, promotion and implementation of the Three Rs and could play a more proactive role in identifying best practice and helping to facilitate exchange of information. When the ERP was established in 1999, one of its main objectives was to promote the application of the Three Rs (see paragraph 13.23). However, in practice, many ERPs focus on the review of licence applications, and although this includes consideration of the Three Rs in relation to the specific project, there is potential for a more general contribution. For example, some ERPs have dedicated Three Rs groups that review husbandry and procedural issues. We acknowledge that some organisations, particularly the LASA and the RSPCA, have organised meetings for ERP members in the past to assist this process. We support this approach and **recommend that these two organisations, together with other stakeholders where appropriate, identify a systematic and sustainable strategy to ensure that the ERP contributes most effectively to developing best practice in the Three Rs**.

Examination of new technologies for Three R potential: Chair of the Three Rs

15.61 We have described the complex interplay leading to the development of Replacements in Chapter 11. Strategic examination of new scientific technologies for Replacement potential, their adaptation for general use and transfer of the technology could help to ensure further progress. Scientists working in basic research who develop new methods for specific research questions often do not have the Refinement, Reduction or Replacement of animal experiments as their main objective and tend not to adapt or promote new methods for this purpose. Much more 'horizon scanning' is needed. The Working Party has therefore considered whether it would be useful to institute at least one Chair of the Three Rs, to undertake research on new technologies for Refinement, Reduction and Replacement potential and to encourage students to carry out research with an emphasis on alternative methods. Several issues would need to be assessed in more detail before such a proposal could be developed further. First, the relationship of the Chair to existing initiatives and organisations that seek to promote the Three Rs would need to be clarified, to avoid duplication of effort, and to ensure that funds to promote the Three Rs are spent most effectively. Secondly, the exact profile of the Chair would need to be carefully defined, to assess whether it would be more appropriate to focus the review of the wide range of new technologies in different areas of research on one of the Three Rs only, for example on Replacement. We have therefore not been able to agree on whether or not a Chair would advance and contribute to increased implementation of the Three Rs. However, **we consider that it would be of value if the MRC, the Wellcome Trust and other major funders of research, in consultation with the NC3Rs, review and explore further the proposal of establishing and funding such a Chair**.

Thorough analysis of scientific barriers to Replacements

15.62 We have considered in Chapter 11 a range of different barriers to Replacements, including regulatory, organisational and resource constraints (paragraphs 11.19–11.30). These difficulties are sometimes cited to dismiss further consideration of Replacement as unfeasible, regardless of the exact objectives of a particular research project. We also observed that some of those opposed to research involving animals claim that a far wider range of research than is commonly assumed could be replaced by alternative non-animal methods, if there was sufficient will to do so (paragraph 11.3). In order to make further progress in the development and the implementation of Replacements, and in order to address the range of associated expectations it would be desirable to undertake a thorough analysis of the scientific barriers to Replacement and how they might be overcome. This task cannot be addressed in general terms, but requires an in-depth analysis of specific projects

in particular areas of research. Since the unavailability of non-animal methods plays a central role in the cost-benefit assessment carried out under the A(SP)A,[32] **we recommend that Ministers request the APC to undertake or commission such an analysis for a series of projects with a wide range of scientific objectives**. A clear exposition of obstacles, and strategies for overcoming them would, first, allow research efforts to be focused on problems that must be overcome if animals are to be replaced for a particular purpose. Secondly, such an analysis would identify publicly the scientific problems which are thought to be insurmountable.

Other issues

15.63 In this section we consider a number of more specific issues:

- ways of motivating and monitoring the reduction of research involving animals (paragraphs 15.65–15.67);
- ways of avoiding duplication of research (paragraphs 15.68–15.70);
- issues raised by the use of GM animals in basic research (paragraphs 15.71–15.75);
- the scientific validity of animal research and the use of animals in the study of human disease (paragraphs 15.76–15.80);
- toxicity testing (paragraphs 15.81–15.83); and
- the international context of research involving animals (paragraphs 15.84–15.91).

Motivating and monitoring the reduction of animal research

15.64 One way of motivating and monitoring any proposed reduction of animal experiments would be to set *targets*. The most radical form of target would be to aim to abandon or phase out a specific area of animal experimentation. As we have said, in the UK the Home Office announced in 1998 that it would not issue any new licences for testing cosmetic products, for the testing of alcohol or tobacco products or for research involving the great apes.[33] More recently, a 7th Amendment to the EU Cosmetics Directive has been approved, which will impose a marketing and sales ban in the EU on cosmetics that have been tested on animals, effective from March 2005.

15.65 Members of the Working Party disagree about the setting of targets. Those who favoured the approach argued that without targets there tends to be drift and fatalism. They emphasised the following:

- Setting targets can focus the mind and encourage determined action. As a heuristic device, the explicit setting of targets can be useful in helping to decide where and how reductions might be achieved.
- The setting of targets is routine in industry, academia and public institutions. It is generally regarded as an essential mechanism to bring about change, and to measure and monitor progress.
- By establishing deadlines, targets can encourage greater and more strategic collaboration in developing alternatives.

32 A(SP)A, Section 5 (a).

33 Animal Procedures Committee (1998) *Press release: Government Announces End To Cosmetic Testing On Animals*, available at: http://www.apc.gov.uk/press_releases/981126b.htm. Accessed on: 1 Apr 2005.

- Ambitious targets might result in the faster development of alternatives, and could establish a country (such as the UK) as a world leader in this area.

15.66 Those who have major reservations with regard to the setting of targets question the feasibility of the approach and assert that those accountable can be unfairly held responsible for unrealistic expectations. Accordingly they consider the following:

- There may be scientific limitations on what can be achieved without using animals in specific areas of research: hence, while setting targets may be feasible in areas such as cosmetics testing, it may be far more difficult in other areas, especially in basic research.
- There may be also pragmatic difficulties, especially in areas such as basic research, and many questions would have to be addressed. For example, how would the demand for and use of animals by the many different research groups be assessed? If there were support for a gross target (such as 'reduce the number of animal X by 70 percent by year Y', how would such a decision be implemented? How many animals could be used by particular commercial laboratories during that period, and how many by academic researchers? How would different capacities of coping with possible higher costs of implementing Replacement methods be considered in the process?
- There can be no guarantee that targets can be met in all instances: difficulties can arise in the case of sudden emergencies, such as the BSE crisis, which might require an unexpected increase in the use of animals.
- Setting targets could lead to alternatives being introduced too rapidly, before they have been subject to rigorous scientific assessment. This could have damaging implications for progress in scientific research and the protection of human and animal health or the environment, as well as for the credibility of alternative methods.
- If targets are set unilaterally, for example in one country, the research or testing may be exported to other countries.

15.67 We make the following observations:

- We welcome the concept of targets as a useful and universally used means of measuring progress towards specific aims. But we also see problems in applying such a strategy to research involving animals, where, in many cases, the setting of specific quantitative (numerical) targets is felt by researchers using animals to be unhelpful. Instead, we suggest that reduction could be encouraged and monitored by means of a more flexible approach. One way would be to consider qualitative *markers of reduction*, for example, aimed at reducing research that causes substantial suffering. **The Government's Interdepartmental Group on the Three Rs should undertake or commission a feasibility study to identify which kinds of *reduction markers* could be set in particular areas of applied and/or basic research.**
- In principle, reduction markers should only be set if they can be linked to a realistic strategy for developing the necessary Replacement methods that will not compromise the amount and quality of basic and applied biomedical research and testing that would otherwise be licensed by the Home Office. Reduction markers that 'ration discovery' are not compatible with the scientific approach.
- The development of any strategy should primarily be the responsibility of legislative bodies and governments, as should the task of providing the infrastructure and some of the funding to facilitate the process, in close consultation with stakeholders from academia, industry and animal protection groups.
- In implementing reduction markers it is crucial that initiatives at the national level are complemented, although not limited by, initiatives at the international level.

Duplication

15.68 Another area where there may be potential for reduction concerns the avoidance of duplication of research or testing (see paragraphs 12.6 and 15.16). In some areas, this can be achieved simply by better coordination and dissemination of information. For example, a recent report by the European Commission on the *Evaluation of the Active Substances of Plant Protection Products*[34] observed:

> '4.6 … multiple dossiers. Many different dossiers were submitted for the same substances, unnecessarily multiplying the number of evaluations required. While every effort was made to encourage notifiers to create taskforces and to submit a single dossier per substance, it was not always possible to achieve this. For example, there were 35 notifiers for the active substance glyphosate and 11 dossiers were submitted. This proved wasteful of resources, as the Rapporteur Member State (Germany) had to examine each one. In the event, only four dossiers were considered complete and could be assessed in detail. Ideally, there would have been a single dossier. This would have saved resources both for the various notifiers and for the Rapporteur Member State. It would also have resulted in fewer laboratory animals being sacrificed in duplicated testing. While every effort is still being made to encourage notifiers to create taskforces and to submit a single dossier per substance, it is still not always possible to achieve this. A solution could be to introduce provision in the legislation to avoid duplicate testing e.g. action point 5F in the White Paper on a Chemicals Strategy[35] proposes that any duplicate testing on vertebrate animals will not result in an exemption from the duty to reimburse the party that owns the property rights to the first test.'

15.69 While this is a clear and unfortunate example of duplication, it appears that the extent to which duplication occurs, whether internationally or nationally, is difficult to assess. Those suspecting that there is a substantial and avoidable amount of duplication are concerned that academic and commercial competition and the aim of protecting intellectual property rights frequently lead researchers to be reluctant to share data. They also assert that many more examples of insufficient coordination, similar to the one described above, could be given.[36] Those who disagree consider that in general there are sufficient mechanisms in place to ensure the avoidance of duplication, such as the publication of peer-reviewed research in scientific journals and presentation at conferences. They take the view that duplication is unlikely to be a widespread phenomenon because funding bodies only support novel research and because both academic and commercial research institutes need to manage resources efficiently, usually implying that only original research is carried out.

15.70 We cannot explore the question of the extent to which duplication occurs, or the feasibility of devising mechanisms that help to avoid the duplication of research in this Report. But we are clear that, in principle, duplication is unacceptable (paragraph 15.16) and we therefore welcome the approach underlying the UK Government's Inter-Departmental Data Sharing Concordat (paragraph 12.6). The Concordat has recently been reviewed by the Government who commented that the agreement had ensured that 'regulators promote data sharing within the scientific community', noting also that there was no

34 Services of the European Commission (2001) *Technical Annex to Report from the Commission to the European Parliament and the Council on the Evaluation of the active substances of plant protection products, SANCO/2692/2001 of 25 July 2001*, available at: http://europa.eu.int/comm/food/plant/protection/resources/ppp01_ann_en.pdf. Accessed on: 21 Apr 2005.

35 European Commission (2001) *White Paper: Strategy for a future chemicals policy. COM (2001)88 final of 27.2.2001* (Brussels: EC).

36 See, for example: British Union for the Abolition of Vivisection (2004) *Memorandum from the British Union for the Abolition of Vivisection, submission to the Select Committee on Science and Technology*, available at: http://www.publications.parliament.uk/pa/cm200304/cmselect/cmsctech/172/172we20.htm. Accessed on 21 April 2005.

evidence that duplication was 'a significant problem in the UK.'[37] The Working Party has not been able to study the review, and is hence not in a position to comment on the Government's view.[38] We note that the APC welcomed the Concordat in its 2003 Report *Review of Cost Benefit Assessment in the Use of Animal Research*[39] but cautioned that it is not yet clear how effective it will be in preventing duplication of animal studies. In particular, the APC was concerned about the voluntary nature of the Concordat, and considered whether more binding measures, such as legislation, will be needed to achieve the Concordat's aims. **We endorse the APC's conclusion that the operation and effectiveness of the Concordat should be monitored carefully and reports placed in the public domain.** The Concordat will be reviewed again in 2006. Depending on the outcome of the review, Ministers should explore whether it would be useful to request the APC to undertake a systematic study addressing in more detail specific issues raised by the possible duplication of research. Such a study could complement and develop further the review of the Concordat, for example by assessing the extent of the problem and, where appropriate, identifying strategies for the avoidance of duplication nationally and internationally. Consideration could also be given to the question of whether duplication occurs because some kinds of data are not made publicly available when experiments fail. It would be especially undesirable if researchers wasted time and effort in duplicating experiments that have elsewhere been found to be unsuccessful. The study could also consider whether funding bodies would have a role in sharing or making available information about past or current research, in order to avoid duplication. We consider special issues with regard to avoiding duplication in the case of GM animals in the next section.

The use of GM animals in basic research

15.71 Specific problems in assessing welfare may be raised by relatively novel ways of producing animals, such as genetic modification or cloning. We take the view that the focus of any concern, in the case of all deliberate attempts to influence the genetic basis of animals, should be on the welfare implications in terms of the likely pain, suffering or distress.

15.72 Welfare implications that may be associated with specific ways of producing animals should be assessed as far as possible in advance. In some areas of basic research, such as forward or reverse genetics, welfare assessments are often not straightforward. If such research is deemed desirable, it is important to limit the number of animals produced as far as possible, for example by ensuring good coordination within and between different laboratories and countries. This is especially so in view of estimates that over the next two decades 300,000 new genetic lines of mice could be created, and expectations that the total number of mice that are expected to be used in mutagenesis and phenotyping studies are of the order of several million each year in the UK alone. We also observed that large numbers of animals are used to produce and maintain each line of GM animals (see paragraphs 5.22 and 7.5).

37 Home Office (2005) *Ministerial Response on the Report by the Animals Procedures Committee – Review of Cost Benefit Assessment in the use of animals in research*, p10, available at: http://www.homeoffice.gov.uk/docs4/jw280305flint_banner_report_by_the_animal_procedures_committee.pdf. Accessed on: 21 April 2005.

38 Parliamentary Under Secretary of State Caroline Flint commented in the Government's response of 28 March 2005 to the APC's Report on the cost-benefit assessment that 'the outcome of the review' would be published as an Annex to the Minutes of the Inter-Departmental Group on the Three Rs, see Home Office (2005) *op. cit.* However, the Working Party was not able to consider this document before finalising this Report.

39 Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p52, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

15.73 Documentation of the phenotypic outcomes of genetic modification (i.e. documentation about the way in which animals are affected) can facilitate the future monitoring and assessment of welfare implications experienced by animals produced in the context of forward or reverse genetics (paragraphs 5.18–5.21). A systematic approach to the description of GM phenotypes is crucial for assessing and monitoring welfare implications, and for undertaking thorough cost-benefit assessments. For this reason, **we recommend that more efforts should be made to establish comprehensive ontologies**[40] **in the form of databases for GM animals. These databases should not be restricted to the receipt and dissemination of phenotypic information relevant to the scientific objectives of the research, but should also provide detailed description of associated implications for welfare. Established central databases, such as the Mouse Genome Database (MGD) in the USA,**[41] **should be used as the primary mechanism for archiving and distributing information on GM animals**. The information should be made available on freely accessible websites for the use of the scientific community and interested lay people.

15.74 It is also important to continue to investigate and improve current methods for assessing the phenotypic and welfare status of GM animals. Any terminology and ontology for describing specific welfare implications should be integrated with the emerging phenotype ontologies. We note that current welfare assessment systems vary with regard to the amount of information and the degree of detail being made available.[42] **We recommend that the NC3Rs should consider this variation with a view to advising on the rationalisation and development of phenotype and welfare ontologies and their interrelationships.**

15.75 **We also recommend that scientific journals require the submission of phenotype and associated data about welfare to databases as a condition of acceptance of submitted papers.** Although scientists often routinely submit information about new phenotypes to databases such as MGD, a more systematic approach would be useful in promoting the availability of information about both the phenotype and the implications for welfare, which would help avoid duplication and improve welfare management. Data should be provided according to the requirements of the standardised transgenic mouse nomenclature.[43]

The scientific validity of animal research and the use of animals in the study of human disease

15.76 In Chapters 5-8 we gave a number of examples which illustrated the use of animals as models for human diseases, and for the assessment of effective and safe interventions. We also considered claims about the predictability and transferability of animal experimentation (paragraphs 8.37–8.41, 8.43 and 10.27–10.43) and concurred with the APC that, because of relevant similarities of anatomical, physiological and neurological structures the scientific validity of animal experiments is:

> 'a condition capable of being fulfilled, but has to be judged case by case and subjected to detailed critical evaluation.'[44]

40 An 'ontology' in this context is an explicit formal specification of terms and the relationships among them, used to underpin the construction and querying of databases.

41 See *Mouse Genome Informatics (MGI)*, available at: http://www.informatics.jax.org. Accessed on: 21 Apr 2005.

42 Jegstrup I, Thon R *et al*. (2004) Characterization of transgenic mice - a comparison of protocols for welfare evaluation and phenotype characterization of mice with a suggestion on a future certificate of instruction *Lab Anim* **37**: p1-9.

43 See *Mouse Nomenclature Home Page*, available at: http://www.informatics.jax.org/mgihome//nomen/index.shtml. Accessed on 21 April 2005.

44 Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p26, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

15.77 The question about the scientific validity of animal experimentation for medical purposes is often confused with questions about complex ethical issues. We emphasised in Chapter 3 that the separation of scientific and ethical questions is essential if greater clarity is to be achieved in the debate about research involving animals. We observed that there is a relatively limited number of useful reviews currently available (paragraph 10.46). **In principle, it would therefore be desirable to undertake further systematic reviews and meta-analyses to evaluate more fully the predictability and transferability of animal models** (see paragraph 10.39). We are aware that carrying out such reviews may be complicated by a number of problems.

15.78 First, it may be difficult to assess if an animal experiment failed to yield specific data because the wrong animal model was used or because the study design was flawed. Any proposed review should identify clearly whether there are areas of research in which scientific methodology (for example, statistical analysis) needs to be improved, or whether there is reason to question the scientific validity of using specific animals as models in particular areas of research.

15.79 Secondly, care should be taken when selecting the studies that are analysed in any review, and the reasons for selection must be made explicit to avoid misunderstandings. Problems could arise if, for example, a review focuses exclusively on an area where progress has been difficult, as the results might be interpreted by some as suggesting that animal research *in general* yields insufficiently transferable results. Similarly, reviews that focus exclusively on areas where progress has been relatively straightforward might be interpreted as proof that *all* animal research yields useful and directly applicable results. Clearly, such interpretations are not useful and contrary to the evidence presented in Chapters 5–9.

15.80 On balance, we consider that there is merit in undertaking appropriately designed and presented reviews on the scientific validity of animal research in specific areas. Since the scientific evaluation of animal research is fundamental to the cost-benefit assessment of any research, **we recommend that the Home Office, in collaboration with major funders of research such as the Wellcome Trust, the MRC, the BBSRC, animal protection groups and industry associations such as the ABPI, should consider ways of funding and carrying out these reviews. In devising a strategy, priorities should be identified which, in order to respond to concerns of the public, consider, among other things, the validity of research that falls in the substantial category, and research that involves primates**.

Testing for toxicity

15.81 Current trends in society suggest that there is an increasing intolerance to risk, although some commentators believe we are now over-zealous in testing requirements.[45] We described the types of procedures typically undertaken in toxicology research in paragraphs 9.9–9.25. In view of the severity that some toxicity testing can entail, **we endorse the recommendation of the House of Lords Select Committee *Report on Animals in Scientific Procedures* (2002) that 'the government and the scientific community should engage more in a systematic and visible search for methods involving the Three Rs in toxicology. The Government should nominate one department to take the lead in this.' We recommend that the Inter-Departmental Group on the Three Rs should coordinate this work**.

15.82 With regard to international initiatives the Working Party is concerned about the potential impact of recent EU legislation for new and existing chemicals testing (REACH), which is likely to be implemented by 2006. According to some estimates, had the initial proposal been implemented, up to 12.8 million animals could have been involved for the testing of

45 For example, Durodie B (2003) The true cost of precautionary chemicals regulation *Risk Anal* **23**(2): 389–98.

approximately 30,000 existing chemicals (see Box 9.2).[46] The conclusion that the scale of testing and use of animals did not appear to justify the additional protection afforded to society has been widely supported, and discussions about the actual implementation were still in progress at the time of writing. Whatever its final form, REACH will greatly increase animal testing across the EU. While we make no detailed recommendation in this area, it is crucial that new approaches to risk assessment that implement the Three Rs most effectively should be explored, particularly by making maximum use of data sharing (paragraphs 15.68 and 15.70), and using computational and *in vitro* tissue culture methods where possible.

15.83 There has been particular concern about toxicity testing of what many perceive to be trivial products, such as cosmetics and toiletry products, or medicines which are very similar to those already on the market.[47] All members of the Working Party who, in principle, can accept some forms of research involving animals, agree that unnecessary testing must be avoided. However, they were not able to agree on specific recommendations because it is not always straightforward to define a trivial use or a form of unnecessary testing. In the case of medicines, improvements are sometimes made in small increments, and although new medicines may differ only slightly from products already marketed, they may in fact be safer or more effective for particular people (see paragraphs 3.13 and 14.40). In the case of cosmetics or toiletry products there is the possibility that some people have sensitivities or allergies towards ingredients such as colorants which different manufacturers use in addition to the active ingredient. Some would therefore argue that a range of apparently identical products can be justified, since the different compositions help to take into account the variability in sensitivities among different people.

The international context of animal research

Problems in harmonising international test guidelines

15.84 Many tests involving animals are conducted to provide safety or efficacy data for regulatory authorities, in compliance with national or international legislation (see paragraphs 9.4 and 13.49–13.52). Thus, if various authorities require testing to be carried out using different study designs, a single chemical that is marketed in a number of countries might need to be tested several times. Harmonisation of test guidelines, so that a single study design is acceptable to regulatory authorities in many countries, is a very valuable means of reducing the use of animals in safety and efficacy testing. The ICH has managed to improve mutual acceptance for the pharmaceutical industry, but much still needs to be done to extend this approach to other product areas.

15.85 In theory, the adoption of guidelines on toxicity testing by the OECD should allow national or supranational regulatory authorities (such as the EPA (Environmental Protection Agency) or FDA (Food and Drug Administration) in the USA, or the European Commission) to incorporate them with minimal change into their own testing requirements. But in practice this has not always been the case. While, the European Commission incorporated new *in vitro* methods for skin corrosivity more than a year before their final review and approval by the OECD, the EPA made changes to the protocols for the three new *in vivo* methods for acute oral toxicity and also to a new OECD-approved *in vivo* method for predicting skin sensitisation (the mouse local lymph node assay). Thus, the EPA delayed acceptance for some time after their adoption by OECD and, in addition, the EPA's requirements for acute

46 Institute for Environment and Health (2001) *Testing requirements for proposals under the EC White Paper – Strategy for future chemicals policy* available at: http://www.le.ac.uk/ieh/webpub/webpub.html. Accessed on: 21 Apr 2005.

47 These medicines are sometimes also referred to as *me-too medicines*.

oral toxicity and skin sensitisation are no longer harmonised with those of other OECD Member States.

15.86 The lack of stringent international harmonisation poses problems. In the UK, the Home Office may only grant a project licence for safety assessment according to the use of procedures that are less severe to the animals involved than those described in a relevant OECD test guideline. This approach means that any company intending to register a product such as an agrochemical formulation in the USA is unable to conduct in the UK a substantial number of the tests required by the EPA. In addition, as most companies have policies for animal welfare that encourage the conduct of a single set of safety tests for global registration, the more severe protocols required by the EPA[48] are usually used and, in the case of UK-based companies, some or all of the testing has to be exported to other countries. There are many other examples of individual countries having different safety requirements.[49] Increased efforts must be made to standardise and harmonise testing requirements, in order to ensure that the minimum number of animals is used at the global level. **We therefore recommend that the UK through its National Coordinators at the OECD makes it a priority to identify areas in which harmonisation continues to be difficult and initiates steps to increase adoption of scientifically valid protocols that entail the least adverse welfare costs to the animals involved.** We also note that under the Inter-Departmental Concordat on data sharing, regulatory authorities aim to 'press for agreement on behalf of the UK Government for fullest provisions and procedures which enable data sharing when negotiating, updating and transposing relevant European Directives and when taking part in other international harmonisation processes'. **In order to support the proposed initiative by the National Coordinators at the OECD, we recommend that the UK Inter-Departmental Group on the Three Rs should produce or commission a report on cases where less severe protocols are not recognised internationally, whether for scientific or other reasons, and make suggestions for improving acceptance.**

15.87 International guidelines also have a crucial role with regard to welfare standards of animals involved in research. There is evidence that relevant OECD guidelines do not use important concepts such as what defines a *maximum tolerated dose, severe distress, obvious pain* or a *moribund condition* consistently (paragraph 9.35).[50] Several of the existing OECD test guidelines could also be improved with regard to issues such as environmental enrichment, and conditions of housing, as, for example, some do not specify the requirement for group housing where this would be possible.[51] All these factors can act as potential sources of avoidable suffering for the animals, and **we recommend that the OECD reviews and revises relevant guidelines to achieve greater consistency and to contribute to a wider application of the Three Rs in view of current knowledge.**

UK researchers commissioning or undertaking research abroad

15.88 There are a number of scientific, Three R-related and logistical reasons why researchers may collaborate with overseas scientists, outsource research work or obtain animals or animal-

48 For example, the use of higher dose levels in the acute oral toxicity tests and additional animals in the local lymph node assay.

49 For example, certain non-OECD countries can still demand an LD50 test, and Japan requires additional safety pharmacology tests (both *in vitro* and *in vivo*) of active ingredients for pesticides.

50 Koeter HBWM (1999) The OECD Test Guidelines Programme and animal welfare concern: how to avoid major animal suffering, in *Humane Endpoints in Animal Experiments for Biomedical Research*, Hendriksen CFM and Morton DB (Editors) (London: Royal Society of Medicine Press), pp13–14.

51 Combes RD, Gaunt I and Balls M (2004) A scientific and animal welfare assessment of the OECD health effects test guidelines for the safety testing of chemicals under the European Union REACH system *ATLA* **32**: 163–208.

derived products (such as monoclonal antibodies) from other countries. This interaction can provide a useful means of disseminating good practice developed within the UK. But there is also a need to ensure that the international nature of research is not used to introduce double standards. **We note the position statement by the Wellcome Trust, which, as a general rule, we endorse:**

> 'International research supported by the Trust is expected to be carried out in the spirit of the UK legislation as well as being compliant with all local legislation and ethical review procedures.'[52]

15.89 Further to the requirement implied in this statement, some members of the Working Party would like to see formal provisions in place which ensure that research and testing, both nationally and internationally, are always carried out in accordance with the least-severe protocols, in order to minimise harm to animals used in research. They would also welcome the introduction of regulations that would prevent UK researchers from importing or outsourcing research or research products that it would not be possible to obtain in the UK. Since the extent to which this may be occurring is uncertain, they would like to recommend that Ministers request the APC to undertake a systematic study to clarify the matter, exploring perhaps also whether a system of certification or voluntary codes of conduct would be suitable devices to ensure that UK-based researchers adhere to the same standards abroad as in the UK. From their point of view, whenever UK researchers are involved in international collaborations they should seek to adopt protocols that meet the highest international standards of best practice. As a minimum they should meet UK requirements, which in most cases are likely to be stricter than those of other countries. The group would also like to recommend that multinational companies that undertake part of their research in the UK should enforce a single global policy on animal care and welfare that meets the highest international standards of best practice.

15.90 However, other members of the group, while welcoming the aspiration behind such proposals, have reservations about their appropriateness and feasibility. They argue that because of the differences in regulatory systems it would be very complicated to ensure that research facilities abroad, or products sourced from outside of the UK met with Home Office approval. If such approval could not be attained, there would be a risk that research and testing facilities in the UK would be disadvantaged, since the exchange of products such as antisera, passaged tumours or GM lines is crucial to collaboration in fundamental research. Accordingly, they do not see a need to recommend that the APC be asked to undertake a study to advance the debate. Similarly they point out that practical problems may prevent multinational companies from implementing a single harmonised policy on animal care and welfare, both in the medium and long term.

15.91 Members also briefly discussed, but were not able to agree on, the question of whether UK-based research might be driven abroad because of the current, or likely future, regulatory provisions and practice. During our fact-finding meetings and discussions we heard conflicting evidence about this possibility. Some researchers observed that several research projects, and some laboratories, have been moved abroad while others, more frequently pharmaceutical companies, consider that the attractiveness of scientific talent in the UK generally outweighs any regulatory burdens. A range of views was represented among members of the Working Party, with some agreeing with the evidence presented during the fact-finding meetings, and others disagreeing. The latter group found arguments

52 The Wellcome Trust *Policy on the use of animals in medical and veterinary research*, available at http://www.wellcome.ac.uk/doc%5Fwtd002764.html. Accessed on: 21 Apr 2005.

against regulation unhelpful especially in view of the fact that those wishing to relax regulations often point to the strictness of the regulatory framework in order to allay concerns, for example, by members of the public. Despite these disagreements, all members of the Working Party emphasise that maintaining high standards in the UK has the potential to continue to influence regulations positively elsewhere. At the same time, the provisions of the A(SP)A and their implementation also need to be reviewed regularly in the context of national and international developments in policy and public debate.